Risk Assessment

Selected Methods of Assessing Human Health & Safety Risk

Environmental Health Risk Approach

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ICF CONSULTING

Risk Assessment

Environmental Health Paradigm

- Similar to the *Chain of Infection*
- Must occur and include a contaminant *Source*, *Mediation* process, and a susceptible *Receptor*

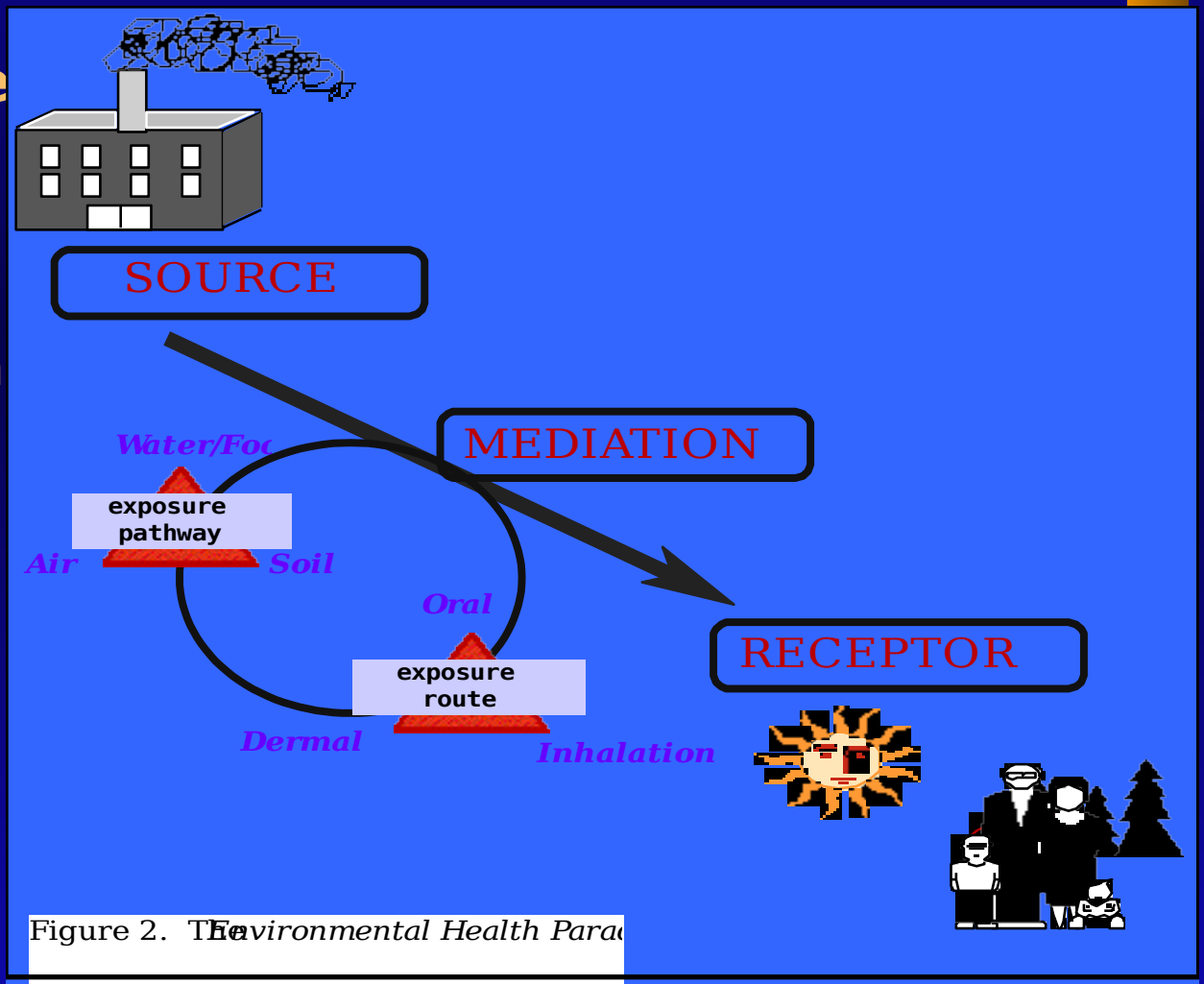


Figure 2. The Environmental Health Para

Risk Assessment

Many U.S. Laws Require or Imply Health Risk Assessments

- Atomic Energy Act
- Clean Air Act
- Clean Water Act
- Consumer Product Safety Act
- Eggs Products Inspection Act
- Federal Food, Drug, and Cosmetics Act
- Federal Hazardous Substances Act
- Toxic Substances Control Act
- Federal Meat Inspection Act
- Federal Mine Safety and Health Act
- Hazardous Liquid Pipeline Safety Act
- Hazardous Materials Transportation Act
- Lead-Based Paint Poisoning Act
- Lead Contamination Control Act of 1988
- Marine Protection, Research, and Sanctuaries Act
- Motor Carrier Safety Act
- National Traffic and Motor Vehicle Safety Act
- Natural Gas Pipeline Safety Act
- Nuclear Waste Policy Act
- Occupational Safety and Health Act
- Poison Prevention Packaging Act
- Poultry Products Inspection Act
- Resource Conservation and Recovery Act
- Safe Drinking Water Act
- Federal Insecticide, Fungicide, and Rodenticide Act
- Comprehensive Environmental Response Compensation and Liability Act (Superfund)

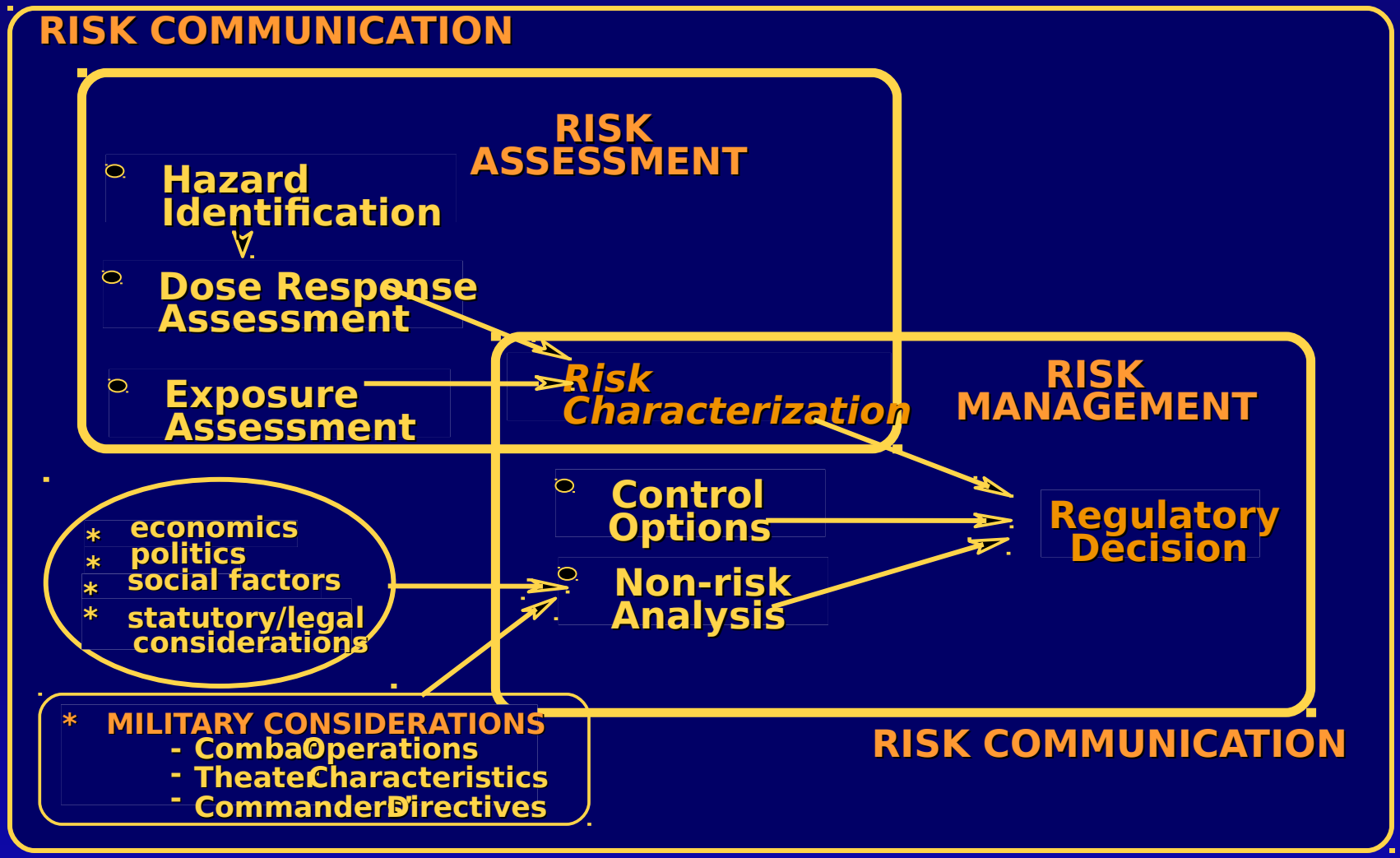
Risk Assessment

The Risk Paradigm

- National Academy of Sciences (1983)
  - Risk Assessment
    - "the characterization of the potential adverse health effects of human exposure to environmental hazards."
  - Risk Management
    - "the judgment and analysis that combine the scientific results of a risk assessment with technology and non-risk factors to produce a decision about environmental action"
  - Risk Communication
    - "informing the public and involving them in the risk assessment and risk management processes."

Risk Assessment

The Risk Paradigm



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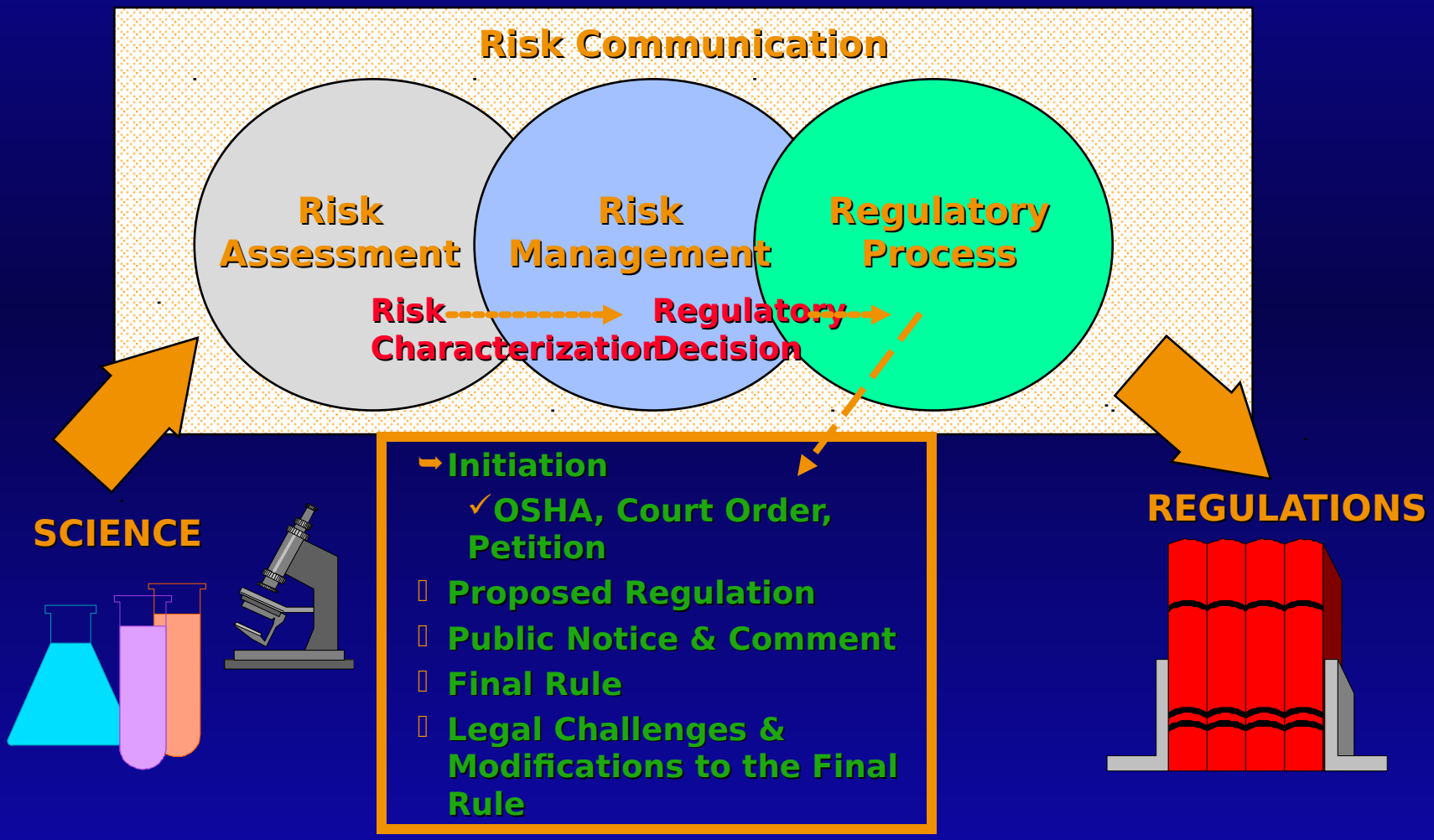
Spectrum: Science to Regulation



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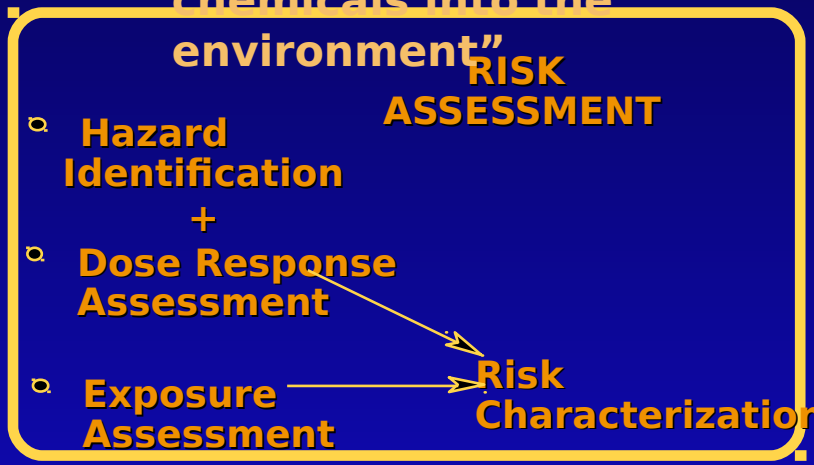
The Risk Assessment Paradigm

- ***Hazard Identification -***
  - "determining whether an agent can cause an increase in the incidence of a health condition (cancer, birth defect, etc.)
- ***Dose-Response Assessment -***
  - "characterizing the relationship between the dose of an agent administered or received and the incidence of an adverse health effects in exposed populations and estimating the incidence of the effect as a function of human exposure to the agent".
- ***Exposure Assessment -***
  - "measuring or estimating the intensity, frequency, and duration of the human exposure to an agent currently present in the environment or of estimating the hypothetical exposure that might arise from the release of new chemicals into the environment"



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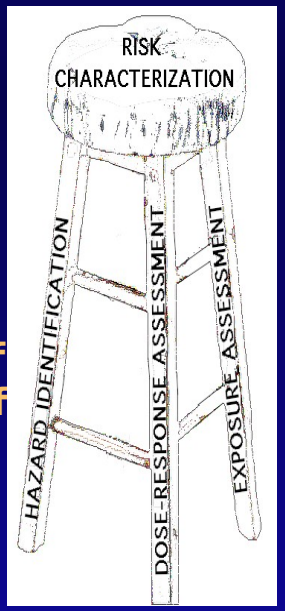
The Risk Assessment Paradigm (continued)

- ***Risk Characterization***
  - estimates the incidence of a health effect under the various conditions of exposure described in exposure assessment
  - performed by combining the hazard identification, exposure assessment, and the dose-response assessment
  - describes the summary effects of the uncertainties in the preceding steps
  - ***Qualitative*** risk characterization
    - Narrative; semi-quantitative terms such as “negligible”, “minimal”, “moderate”, “severe”, “acceptable”.
    - Comparisons to common hazards and risks: “less than”, “equal to”, or “greater than”
  - ***Quantitative*** risk characterization expresses hazard and risk in numerical terms; amount of hazard per unit dose or exposure of an agent, e.g., percent change in response for each milligram of agent per kilogram of animal body weight.
    - Derelanko and Hollinger, *CRC Handbook of Toxicology*, 1995



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Quantitative Risk Characterization - Systemic/Non-cancer Effects

- Reference Dose (RfD) = NOAEL / UF
  - "an estimate (with an uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime"
  - NOAEL-No Observed Adverse Effect Level
  - LOAEL-Lowest Observed Adverse Effect Level
  - UF-Uncertainty Factor

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Risk Assessment Policy Issues: Uncertainty Factors

Basis for UF	General Comments
❖Human (Intraspecies)	10-fold factor for variability in human populations
❖Animal (Interspecies)	10-fold factor for differences in responses between animals and humans.
❖Subchronic to Chronic	10-fold factor when chronic data are unavailable and a 90- day study is used
❖LOAEL to NOAEL	10-fold factor when LOAEL instead of NOAEL is used
❖Data Gaps	3- to 10-fold factor is applied for “Incomplete” data bases (i.e., missing studies).
❖Modifying Factor	Usually applied for differences in absorption rates, tolerance to a chemical, lack of sensitive endpoint, or other toxicokinetics/dynamic parameters. The default value is 1.

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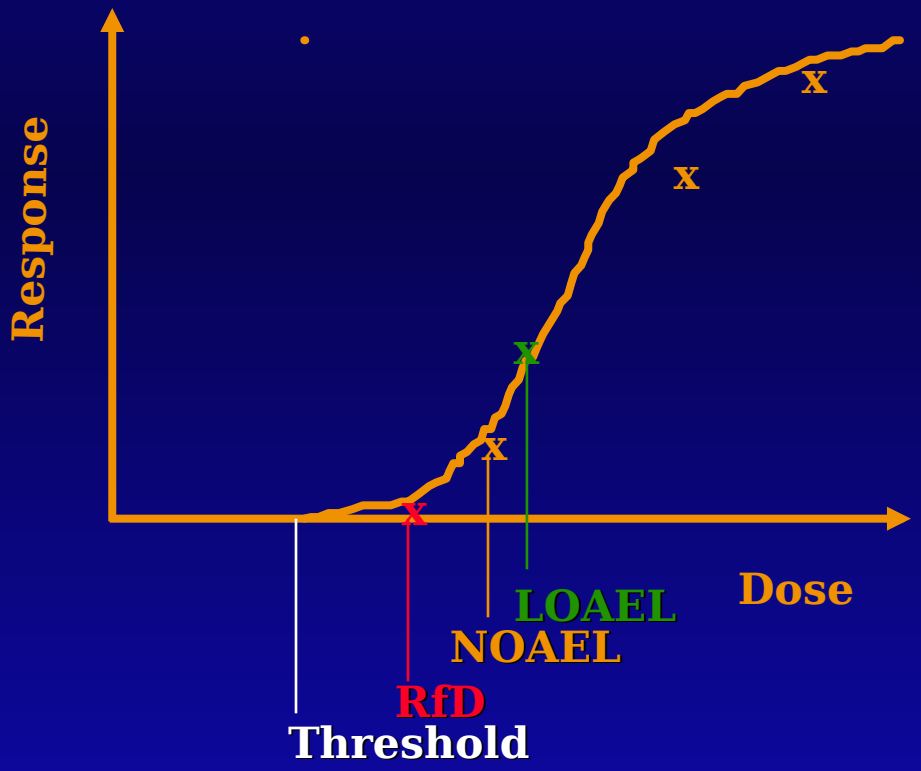
Quantitative Risk Characterization Threshold Dose-Response Example

- Dose-Response Relationships



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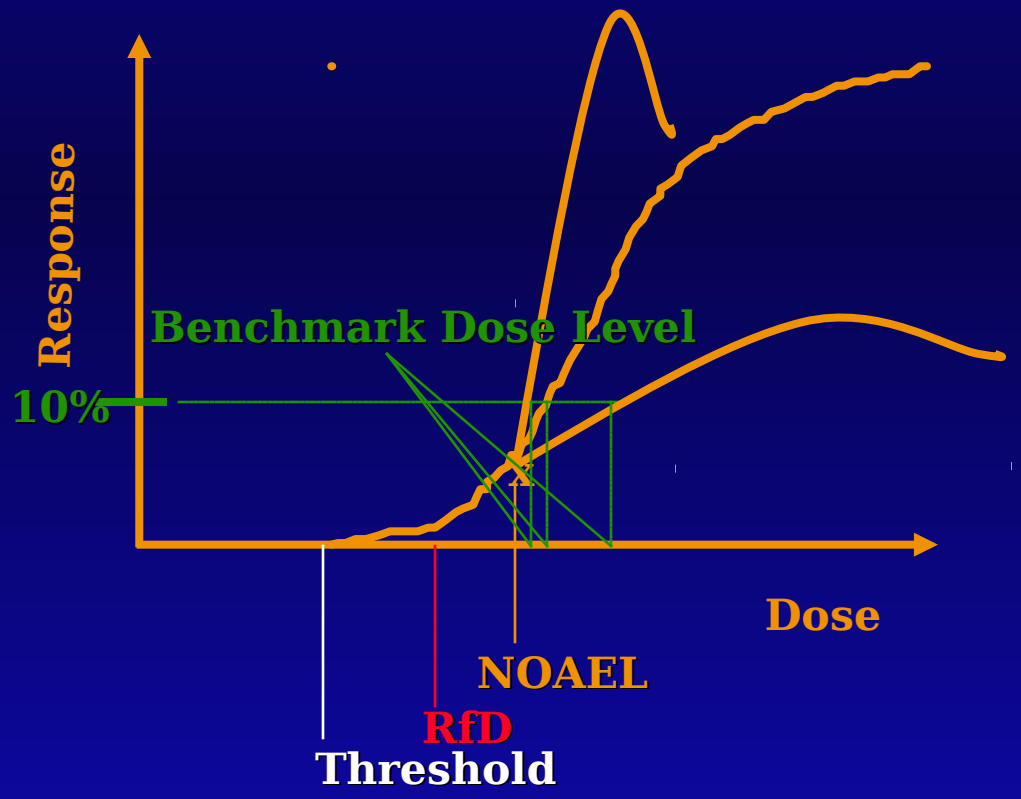
Quantitative Risk Characterization Threshold Dose-Response Example

- Dose-Response Relationships



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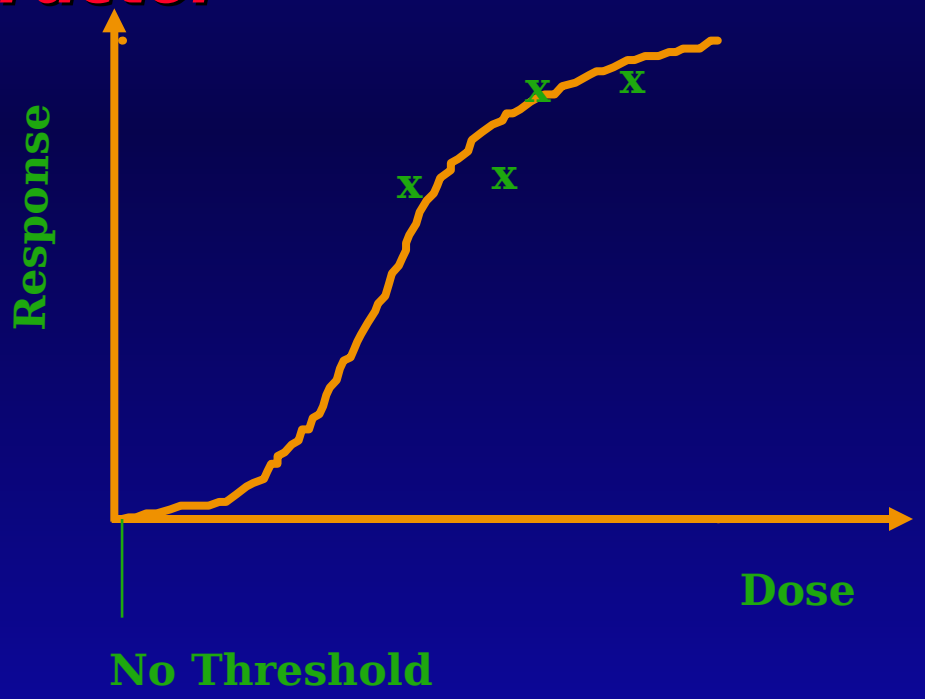
Quantitative Risk Characterization Cancer Risk Estimate (Nonthreshold)

- Cancer Potency Factor
  - …also, ***Slope Factor***
  - …also, q_1^*



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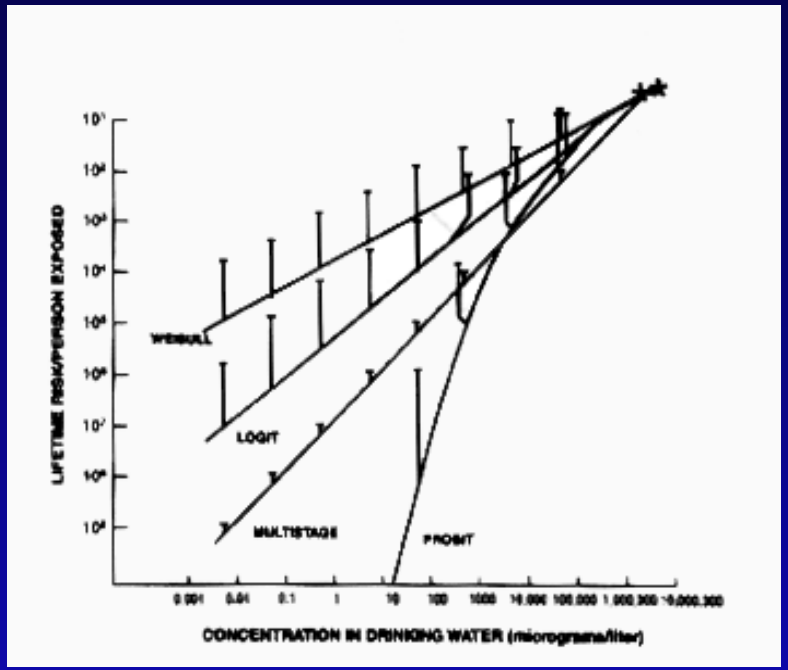
Risk Assessment Policy Issues: Carcinogenicity

- Models
  - One-hit
  - Multihit
  - Weibull
  - Multistage
  - Linearized Multistage
  - Logit
  - Probit
- Classifications
  - EPA
  - OSHA
  - IARC



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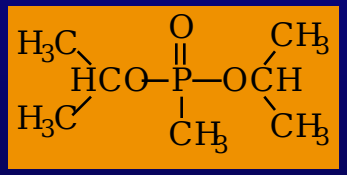
Example Diisopropyl Methylphoshonate (DIMP)

- Dog (beagle)
  - 0, 3.75, 37.5, 75 mg/kg/day x 90 days
  - No effects at highest dose
  - NOAEL = 75 mg/kg/day
  - EPA: RfD = 75 mg/kg/day÷1000 UF = 0.075 mg/kg/day



- Mink
  - 0, 11, 37, 95 mg/kg/day x 12 months
  - Significant increased mortality in high dose group
  - High natural mortality? “Known high annual mortality and lack of information on this species limit the use of this study for human health assessment.”
  - Colorado State: 80,000 UF???

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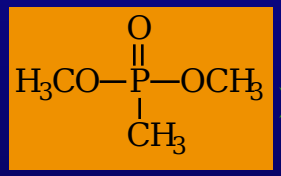
Example Diisopropyl Methylphoshonate (DIMP)



- Dimethyl methylphosphonate (DMMP)
  - Tumor Type: Mononuclear Cell Leukemia, Kidney Transitional Cell Papillomas and Carcinoma
  - Test Animals: Rat, F344/N M

  - Route: Oral/Gavage
  - Reference: NTP (1987)

Dose (mg/kg/day)			Tumor Incidence
Administered	Human Equivalent*, **		
	Surface Area*	Body Weight**	
0	0	0	10/43
357	67	8	18/41
714	130	15	20/43

- * Administered Dose ÷ (70 kg/rat weight)$^{1/3}$
- ** Administered Dose ÷ (70 kg/rat weight)$^{3/4}$
- Rat weights were averaged from study day 44 to 105 and were 0.476 kg, 0.465 kg, and 0.420 kg for the control, low- and high-dose groups, respectively.

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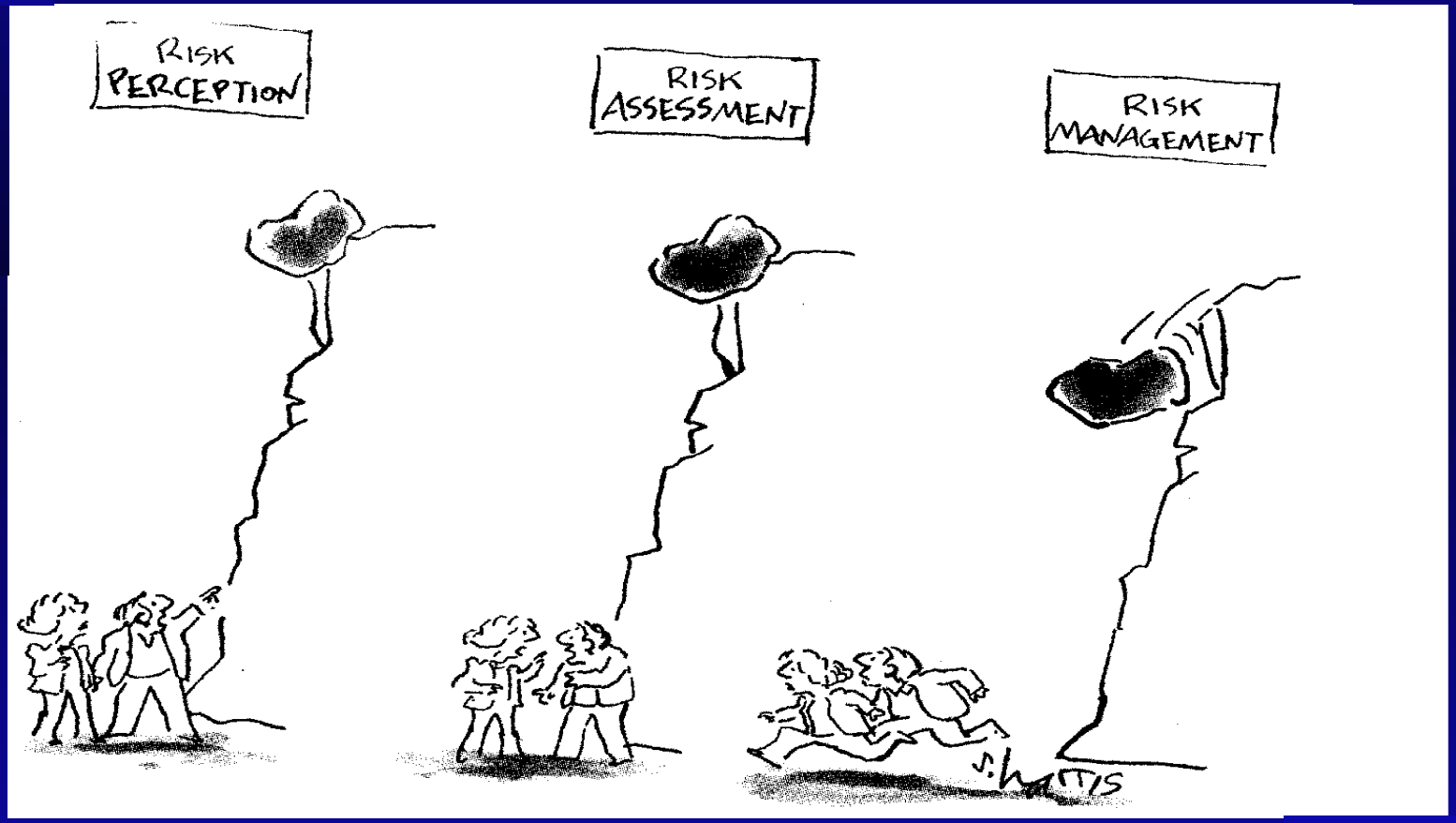
The Focus



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Discussion & Questions & Comments

? Discussion

? Questions

? Comments